REMARKS

Favorable reconsideration of this application, in light of the preceding amendments and following remarks, is respectfully requested.

Claims 24, 31, 37, 39-40, 46-54, 56-58 and 60-64 are pending in this application. Claims 24, 46-54, 56-58 and 60-64 are amended and claims 28-29, 32-36, 59 and 65 have been cancelled. Claims 24 and 46 are the independent claims.

Claim Objections

Claim 65 is objected to because the claim language is confusing due to the wording of the claim. Applicants have cancelled claim 65, and therefore, the objection to claim 65 is now moot.

Example Embodiments

Example embodiments recite a DNA fragment for causing a cell to produce an arbitrary protein including cDNA of a virus vector that has been constructed by inserting a coding gene of an arbitrary protein into an RNA virus, a ribozyme sequence ligated to the 3' end of the virus vector cDNA, and a gene that encodes a transcription factor for controlling transcription induced by an inducible promoter that is located upstream of the virus vector cDNA and the ribozyme sequence, wherein the virus vector includes a tomato mosaic virus vector, the ribozyme sequence includes a ribozyme sequence of satellite tobacco ringspot virus, the cDNA of the virus vector in which the coding gene of an arbitrary protein has been incorporated, and the ribozyme sequence ligated to the 3' end of the virus vector cDNA are transcribed under control of the inducible promoter,

and the transcription is controlled by (i) GVG, and (ii) 6XUASga14, which is a promoter induced by activated GVG.

Usually, a plasmid vector is employed in a plant such that an enhanced expression efficiency is obtained. Use of a virus vector, on the other hand, tends to cause a deterioration in an expression efficiency. As illustrated in FIG. 7 and other examples of the present application, an effect of example embodiments is higher expression efficiency of 60% (even using a virus vector) due to the ligation of the ribozyme sequence to the 3' end of the virus vector and the transformation step being performed in multiple stages.

The following description explains in detail a reason why a plant culture cell line showing expression efficiency of nearly 100 % can be obtained. In Example 3 in the Specification of the subject application, it is described that, among the three transformant cell lines (ERS-17, ERS-20, and ERS-3) which were obtained through the first transforming step, the screening step, and the second transforming step, any transformant cell line having 1 % or more individual transformant cells emitting GFP fluorescence was selected as the highly-expressing cell line.

The specific step of the procedure included callusing the three transformant cell lines obtained after the second transforming step. Then, the resultant calluses were cultured in liquid culture media, and bred over generations in such a manner that individual transformant in each of the three transformant cell lines was 1 / 100 (see pages 30-31 of the specification as filed). The individual transformant cells were caused to express GFP, and then observed with the microscope so that the number of individual transformant cells emitting GFP fluorescence could be counted. Within one microscope filed, generally, roughly 100 through 300 individual transformant cells could be observed. Thus, any of the three

transformant cell lines which had 1 through 3 or more individual transformant cells emitting GFP fluorescence was selected as the highly-expressing cell line. The result of this was as shown in Table 1 (see page 67 of the specification as filed).

Since any of the three transformant cell lines which had at least 1 % individual transformant cells emitting CFP fluorescence was selected as the "highly-expressing cell line", the selected transformant cell lines included a. line of variation which had 10 % individual transformant cells emitting GFP fluorescence, another line of variation which had approximately 50 % individual transformant cells emitting GFP fluorescence, and still another line of variation which had approximately 100 % individual transformant cells emitting GFP fluorescence. Particularly, like ES-20 shown in Table 1, in any transformant cell line whose 30 % or more lines of variation were selected as the highly-expressing cell lines, it was empirically highly probable that some of the selected line of variation had 100 % individual transformant cells emitting GFP fluorescence. Thus, by further culturing over generations 33 lines of variation of ER8-20 selected as the GFP highly-expressing lines and repeatedly screening resultant culture lines, it is possible to eventually obtain, a few cell lines having expression efficiency of approximately 100 %.

Furthermore, example embodiments provide for transforming steps at two different stages, which prevents or reduces the possibility of a protein becoming chimeric such that the expression of a function of the protein is improved.

Rejections under 35 U.S.C. § 102(b)

Garger

Claims 24, 28, 29, 31, 37, 39 and 40 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Garger et al. (U.S. Patent Publication No. 2002/0061309,

hereinafter "Garger"). Applicants respectfully traverse this rejection for the reasons detailed below.

On page 3 of the Office Action, the Examiner states that Garger teaches a DNA molecule comprising cDNA of a tobacco mosaic virus vector that contains a coding sequence of a protein fused to the native coat protein coding sequence, where the 3' end of the viral cDNA is immediately followed by a self-processing ribozyme sequence from satellite tobacco ringspot virus RNA. Applicants respectfully disagree.

Applicants submit that Garger does not teach or suggest all of the limitations of claim 24. In particular, Garger does not teach or suggest the virus vector includes a tomato mosaic virus vector, the cDNA of the virus vector in which the coding gene of an arbitrary protein has been incorporated, and the ribozyme sequence ligated to the 3' end of the virus vector cDNA are transcribed under control of the inducible promoter, and the transcription is controlled by (i) GVG, and (ii) 6XUASga14, which is a promoter induced by activated GVG as recited in claim 24.

The Applicants, therefore, respectfully request that the rejection to Claim 24 under 35 U.S.C. § 102(b) be withdrawn.

Claims 28-29, 31, 37 and 39-40, dependent on independent claim 24, are patentable for the reasons stated above with respect to claim 24 as well as for their own merits.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection to independent claim 24 and all claims dependent thereon.

Rejections under 35 U.S.C. § 103

Garger in view of Zuo

Claims 32-36 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Garger et al. (U.S. Patent Publication No. 2002/0061309) in view of Zuo et al. (U.S. Patent No. 6,452, 068).

Even assuming *arguendo* that Zuo could be combined with Garger (which Applicants do not admit), the Examiner has failed to show how Zuo remedies the deficiencies of Garger with respect to independent claim 24. Thus, claims 32-36, dependent on independent claim 24, are patentable over Garger and Zuo for the reasons set forth above with respect to independent claim 24.

The Applicants, therefore, respectfully request that the rejection to Claims 32-36 under 35 U.S.C. § 103(a) be withdrawn.

Mori in view of David

Claims 46-48, 50, 51, and 56-64 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Mori et al. (The Plant Journal, Vol. 27, No. 1, pages 79-86, 2001) in view of David et al. (Plant Physiology, Vol. 125, pages 1548-1553, April 2001). Applicants respectfully traverse this rejection for the reasons detailed below.

On page 9 of the Office Action, the Examiner admits that Mori does not teach a method where the GVG transformants are further transformed with the cDNA of a virus vector that encodes IFN using an Agrobacterium method nor that the cells are tobacco BY-2 cells and relies on David for these features of claim 46. Applicants respectfully disagree.

Conventionally, transformation of a plant by use of a virus vector has been difficult. That is, even in a case where the plant is transfected with multiple

genes by using a single virus vector, expression efficiency of the multiple genes is very low. Such a problem does not arise if no virus vector is employed, i.e., if a vector other than a virus vector, e.g., plasmid, is employed. In other words, the problem arises selectively in a case where a virus vector is employed. Further, the problem is more serious in a case where a plant culture cell is transformed than in a case where a plant is transformed.

For example, in a case where a plant culture cell is transfected with (i) a GFP gene and (ii) a transcription factor for transcription induction by using a single plasmid, an expression efficiency (a ratio of cells which emit light) to be obtained is approximately 100%. Also, in a case where a plant is transfected with (i) and (ii) by using a single plasmid, expression efficiency to be obtained is approximately 100 %. On the other hand, in, a case where a plant is transfected with (i) and (ii) by using a single virus vector, expression efficiency to be obtained is approximately 30 % at maximum. Expression efficiency is further lowered to be less than 5 % in a case where a plant culture cell is transfected with (i) and (ii) by using a single virus vector (see the result of the use of the control vector in Example 2 in the Specification of the subject application).

Applicants respectfully submit that an improved expression efficiency, i.e., 60%, would not be achieved in the references cited as neither of the references insert a virus vector at two different stages as is recited in independent claim 46. Further, when transforming a plant by using a normal vector such as a plasmid, one skilled in the art would not be motivated to employ a time- and effort-consuming "serial transforming method" as the method of claim 46, especially when the efficiency of transformation in which a plant is transformed by using a single vector is satisfactorily high.

For example, Mori crosses a GVG-expressing plant with a 2FR-expressing plant, unlike the method of claim 46. David expresses a target protein by inserting a plasmid at two stages. However, neither David, Mori nor the combination thereof describes inserting a transcription factor at a first step and then inserting a DNA fragment coding a virus vector at a second step as recited in claim 46, which allows for expression of a protein carried in the virus vector at a last step of procedure.

that takes place in two different stages as recited in claim 46.

With regards to the combination of Mori and David, Applicants respectfully submit that one skilled in the art would recognize the unpredictability of adding a second transforming step as disclosed in David to the process of Mori in order to render obvious the process of claim 46. David transforms a plasmid at two different stages, but as explained previously, a normal plasmid and virus vector are different from each other in terms of efficient expression. Therefore, Applicants submit that an additional transforming step as disclosed in David may not be simply added to the process as disclosed in Mori because there is no teaching of how an additional transforming step including a virus vector may be implemented in the process of Mori or David.

Furthermore, Applicants respectfully submit that the Examiner does not provide a clear rationale including articulated reasoning that one of ordinary skill in the art would have been motivated to make the proposed combination of Mori and David. Instead, the Examiner makes the conclusory statement that it would have been obvious to one skilled in the art to make the proposed combination of references, e.g., Mori and David, given the expected benefit of selecting BY2GVG transformants with desirable levels of GVG expression prior to transformation with the IFN

expression vector, and that BY2 cells have an exceptionally high growth rate and are easy to transform.

However, without a clear rationale for making the proposed combination, the Examiner could render obvious every combination, and a requirement for some technical or logical motivation absent guidance provided by the present specification for making the combination would be effectively removed. See MPEP § 2143.01; citing *Ex parte Levengood*, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993) ("[a] statement that modifications of the prior art to meet the claimed invention would have been 'well within the ordinary skill of the art at the time the claimed invention was made' because the references relied upon teach that all aspects of the claimed invention were individually known in the art is not sufficient to establish a *prima facie* case of obviousness without some objective reason to combine the teachings of the references") and *In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006) ("[r]ejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.").

As the Examiner has not made a prima facie case of obviousness for combining Mori and David, Applicants submit that claim 46 has not been rendered obvious in view of the cited references.

The Applicants, therefore, respectfully request that the rejection to Claim 46 under 35 U.S.C. § 103(a) be withdrawn.

Claims 47-48, 50, 51, and 56-64, dependent on independent claim 46, are patentable for the reasons stated above with respect to claim 46 as well as for their own merits.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection to independent claim 46 and all claims dependent thereon.

Mori in view of David and Zuo

Claim 49 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over Mori et al. The Plant Journal, Vol. 27, No. 1, pages 79-86, 2001) in view of David et al. (Plant Physiology, Vol. 125, pages 1548-1553, April 2001), and further in view of Zuo et al. (U.S. Patent No. 6,452,068).

Even assuming *arguendo* that David and Zuo could be combined with Mori (which Applicants do not admit), the Examiner has failed to show how David and Zuo remedies the deficiencies of Mori with respect to independent claim 46. Thus, claim 49, dependent on independent claim 46, is patentable over Mori, David and Zuo for the reasons set forth above with respect to independent claim 46.

The Applicants, therefore, respectfully request that the rejection to Claim 49 under 35 U.S.C. § 103(a) be withdrawn.

Mori in view of David and Rasochova

Claims 52-54 stand rejected under 35 U.S.C. § 103(a) as being unpatentable Mori et al. The Plant Journal, Vol. 27, No. 1, pages 79-86, 2001) in view of David et al. (Plant Physiology, Vol. 125, pages 1548-1553, April 2001), and further in view of Rasochova et al. (U.S. Patent Publication No. 2003/0074677).

Even assuming *arguendo* that David and Rasochova could be combined with Mori (which Applicants do not admit), the Examiner has failed to show how David and Rasochova remedy the deficiencies of Mori with respect to independent claim 46. Thus, claims 52-54, dependent on independent claim 46, are patentable over Mori,

David and Rasochova for the reasons set forth above with respect to independent claim 46.

The Applicants, therefore, respectfully request that the rejection to Claims 52-54 under 35 U.S.C. § 103(a) be withdrawn.

Garger in view of Martinez

Claims 32-34 and 65 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Garger et al. (U.S. Patent Publication No. 2002/0061309) in view of Martinez et al. (The Plant Journal, Vol. 19, No. 1, pages 97-106, 1999).

Even assuming *arguendo* that Martinez could be combined with Garger (which Applicants do not admit), the Examiner has failed to show how Martinez remedies the deficiencies of Garger with respect to independent claim 24. Thus, claims 32-34 and 65, dependent on independent claim 24, are patentable over Garger and Martinez for the reasons set forth above with respect to independent claim 24.

The Applicants, therefore, respectfully request that the rejection to Claims 32-34 and 65 under 35 U.S.C. § 103(a) be withdrawn.

CONCLUSION

Accordingly, in view of the above amendments and remarks, reconsideration of the objections and rejections and allowance of each of claims in connection with the present application is earnestly solicited.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Donald J. Daley at the telephone number of the undersigned below.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 08-0750 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. §1.17; particularly, extension of time fees.

Respectfully submitted,

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